FILE 'HOME' ENTERED AT 11:16:56 ON 31 MAY 2002

=> file medline caplus embase biosis
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.21 0.21

FILE 'MEDLINE' ENTERED AT 11:17:10 ON 31 MAY 2002

FILE 'CAPLUS' ENTERED AT 11:17:10 ON 31 MAY 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE 'EMBASE' ENTERED AT 11:17:10 ON 31 MAY 2002

FILE 'BIOSIS' ENTERED AT 11:17:10 ON 31 MAY 2002

=> s ylsgadinl
L1 0 YLSGADINL

=> s ylsgadlnl
L2 9 YLSGADLNL

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3 3 DUP REM L2 (6 DUPLICATES REMOVED)

=> dis l3 1-1 ibib abs

L3 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:107538 CAPLUS
DOCUMENT NUMBER: 136:149862
TITLE: Modified human carcinoembryonic antigen CAP-1 peptides and their use in cancer vaccines
INVENTOR(S): Berinstein, Neil; Tartaglia, James; Tine, John A.; Panicali, Dennis L.; Gritz, Linda; Schlom, Jeffrey
PATENT ASSIGNEE(S): Aventis Pasteur Limited, Can.; Therion Biologics; National Cancer Institute
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002010379	A2	20020207	WO 2001-CA1092	20010727

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-222043P P 20000731
AB The invention discloses immunogenic CEA (carcinoembryonic antigen) agonist polypeptides/proteins comprising a modified epitope contg. the amino acid sequence **YLSGADLNL**, nucleic acids coding therefor, vectors and/or cells comprising said nucleic acids, and mixts. and/or compns. thereof. Methods for eliciting or inducing CEA-specific immune responses utilizing the aforementioned agents are also disclosed. Use of the modified CEA CAP-1 polypeptide and the nucleic acid sequence encoding it in the treatment of gastrointestinal, breast, pancreatic, ovarian, lung or prostate cancer is provided. Methods for generation of viral vectors encoding the said sequence are provided. These include poxviruses, adenoviruses and alphavirus components.

=>

=> dis l3 2-3 ibib abs

L3 ANSWER 2 OF 3 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000175479 MEDLINE
DOCUMENT NUMBER: 20175479 PubMed ID: 10709104
TITLE: Agonist peptide from a cytotoxic t-lymphocyte epitope of human carcinoembryonic antigen stimulates production of tc1-type cytokines and increases tyrosine phosphorylation more efficiently than cognate peptide.
AUTHOR: Salazar E; Zaremba S; Arlen P M; Tsang K Y; Schlom J
CORPORATE SOURCE: Laboratory of Tumor Immunology and Biology, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892-1750, USA.
SOURCE: INTERNATIONAL JOURNAL OF CANCER, (2000 Mar 15) 85 (6) 829-38.
Journal code: GQU; 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000330
Last Updated on STN: 20000330
Entered Medline: 20000323
AB The identification of an agonist peptide (**YLSGADLNL**, designated CAP1-6D) to an immunodominant cytotoxic T-lymphocyte (CTL) epitope (designated CAP1) of human carcinoembryonic antigen (CEA) has previously been reported. The agonist peptide harbors a single amino acid substitution at a non-MHC anchor residue and is proposed to exert its effects at the level of the T-cell receptor (TCR). The type and magnitude of cytokines produced by CAP1-reactive CTL upon stimulation with the agonist peptide, CAP1-6D, were compared to those obtained upon stimulation with the cognate CAP1 peptide. In addition, early events in the TCR

signaling pathway were examined for differences in tyrosine phosphorylation. Upon stimulation with the agonist peptide CAP1-6D, several different CEA-specific CTL lines exhibited a marked shift in the peptide dose response, which resulted in as much as a 1,000-fold increase in the levels of GM-CSF and gamma-IFN produced as compared with the use of the CAP1 peptide. However, levels of IL-4 and IL-10, which are associated with anti-inflammatory effects, were very low or non-existent. The cytokine profile of CAP1- and CAP1-6D-specific CTL is consistent with a Tc1-type CTL. Consistent with these findings, CEA-specific CTL showed increased tyrosine phosphorylation of TCR signaling proteins ZAP-70 and TCR zeta chains in response to both peptides. However, when CAP1-6D was compared with the wild-type peptide, the increase in ZAP-70 phosphorylation was greater than the increase in zeta phosphorylation. CTL generated with the CAP1-6D agonist were shown capable of lysis of human carcinoma cells expressing native CEA. The ability to upregulate the production of GM-CSF, gamma-IFN, TNFalpha and IL-2 with the agonist peptide, as compared with CAP1, may help in initiating or sustaining anti-tumor immune responses and thus potentially prove to be useful in the treatment of CEA-positive tumors.

L3 ANSWER 3 OF 3 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1998021980 MEDLINE
DOCUMENT NUMBER: 98021980 PubMed ID: 9377571
TITLE: Identification of an enhancer agonist cytotoxic T lymphocyte peptide from human carcinoembryonic antigen.
AUTHOR: Zaremba S; Barzaga E; Zhu M; Soares N; Tsang K Y; Schlom J
CORPORATE SOURCE: Laboratory of Tumor Immunology and Biology, Division of Basic Sciences, National Cancer Institute, Bethesda, Maryland 20892-1750, USA.
SOURCE: CANCER RESEARCH, (1997 Oct 15) 57 (20) 4570-7.
Journal code: CNF; 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971110

AB A vaccination strategy designed to enhance the immunogenicity of self-antigens that are overexpressed in tumor cells is to identify and slightly modify immunodominant epitopes that elicit T-cell responses. The resultant T cells, however, must maintain their ability to recognize the native configuration of the peptide-MHC interaction on the tumor cell target. We used a strategy to enhance the immunogenicity of a human CTL epitope directed against a human self-antigen, which involved the modification of individual amino acid residues predicted to interact with the T-cell receptor; this strategy, moreover, required no prior knowledge of these actual specific interactions. Single amino acid substitutions were introduced to the CAP1 peptide (YLSGANLNL), an immunogenic HLA-A2+-binding peptide derived from human carcinoembryonic antigen (CEA). In this study, four amino acid residues that were predicted to potentially interact with the T-cell receptor of CAP1-specific CTLs were systematically replaced. Analogues were tested for binding to HLA-A2 and for recognition by an established CTL line directed against CAP1. This line was obtained from peripheral blood mononuclear cells from an HLA-A2+ individual vaccinated with a vaccinia-CEA recombinant. An analogue peptide was identified that was capable of sensitizing CAP1-specific CTLs 10(2)-10(3) times more efficiently than the native CAP1 peptide. This enhanced recognition was shown not to be due to better binding to HLA-A2. Therefore, the analogue CAP1-6D (**YLSGADLNL**, Asn at position 6 replaced by Asp) meets the criteria of a CTL enhancer agonist peptide. Both the CAP1-6D and the native CAP1 peptide were compared for the ability to generate specific CTL lines in vitro from unimmunized apparently healthy HLA-A2+ donors. Whereas CAP1 failed to generate CTLs from normal peripheral blood mononuclear cells, the agonist peptide was able to generate CD8+ CTL lines that recognized both the agonist and the native CAP1 sequence. Most importantly, these CTLs were capable of lysing human tumor cells endogenously expressing CEA. The use of enhancer agonist CTL peptides may thus represent a new efficient direction for immunotherapy protocols.

```
=> ylsgadinl
YLSGADINL IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s ylsgadinl
L4            0 YLSGADINL

=> s ylsganonl
L5            0 YLSGANONL

=> s ylsganinl
L6            0 YLSGANINL

=> s ylsgaclnl
L7            0 YLSGACLNL

=> end
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                        ENTRY    SESSION
FULL ESTIMATED COST                                     15.95      16.16

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                        ENTRY    SESSION
CA SUBSCRIBER PRICE                                     -0.62      -0.62

STN INTERNATIONAL LOGOFF AT 11:20:51 ON 31 MAY 2002
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(FILE 'HOME' ENTERED AT 10:52:34 ON 31 MAY 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 10:52:57 ON 31 MAY 2002

L1	1867	S	SCHLOM J?/AU OR BARZAGA E?/AU OR ZAREMBA S?/AU
L2	351	S	L1 AND CEA
L3	0	S	L2 AND YLSGANLN
L4	0	S	YLSGANLN
L5	0	S	L3 AND EPITOP?
L6	89	S	L2 AND EPITOP?
L7	10	S	L6 AND AGONIST
L8	4		DUP REM L7 (6 DUPLICATES REMOVED)
L9	30508	S	CEA
L10	0	S	L9 AND YLSGANINL
L11	1258	S	L9 AND EPITOP?
L12	15	S	L11 AND AGONIST?
L13	7		DUP REM L12 (8 DUPLICATES REMOVED)
L14	3	S	L13 NOT L8